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STATE-OF-THE-ART PAPERS

STATE-OF-THE-ART PAPERS

Genetic Susceptibility to CAD 1715

Robert Roberts, Alexandre F. R. Stewart

Susceptibility of coronary artery disease (CAD) is thought to be 40% to 60% inherited, but the genetic risk factors predisposing to CAD remain undefined. The availability of microarrays of single nucleotide polymorphisms enabling genome-wide association studies (GWAS) led to the discovery of 33 genetic risk variants for CAD. Surprisingly, 23 risk variants mediate their risk through unknown mechanisms, with only 10 associating with hypertension or lipids. The first risk variant discovered by GWAS was 9p21.3 with a mean increased risk of 25% per copy. Roberts and Stewart review the current utility of genetic testing for cardiovascular risk and future directions of this field, which will likely lead to the identification of novel pathways that increase cardiovascular risk independent of diet, sex, age, cholesterol, or blood pressure.

STATE-OF-THE-ART PAPERS

Percutaneous Treatment of PFO and ASDs 1722

Jonathan Tobis, Michael Shenoda

Percutaneous treatment of interatrial septal defects has experienced exponential growth in the past 2 decades. Improved percutaneous devices, interventional techniques, and low complication rates make this procedure an attractive therapeutic option for congenital atrial septal defects (ASDs). Tobis and Shenoda review the anatomy and indications for catheter-based ASD closure. The indications for catheter-based patent foramen ovale (PFO) closure are still evolving. Results from 2 randomized clinical trials question the benefits of percutaneous PFO closure, but the authors review questions raised about the efficacy of the particular device used in the trials and the need for further trials.

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CLINICAL RESEARCH

INTERVENTIONAL CARDIOLOGY

PCB Angioplasty Appears Effective in a Large Prospective Registry **1733**

Jochen Wöhrle, Mariusz Zadura, Sven Möbius-Winkler, Matthias Leschke, Christian Opitz, Waqas Ahmed, Paul Barragan, Jean-Philippe Simon, Graham Cassel, Bruno Scheller

In small randomized trials, paclitaxel coated balloon (PCB) angioplasty was superior to uncoated balloon angioplasty for treatment of bare-metal stent (BMS) and drug-eluting stent (DES) restenosis. Wöhrle and colleagues report the safety and efficacy of PCB angioplasty in an international, multicenter, prospective, registry study. In 75 centers, 2,095 patients were treated with PCB. Target lesion revascularization (TLR) rate was 5.2% after mean 9.4 months; vessel thrombosis occurred in 0.1%. TLR rate was significantly lower in patients with PCB angioplasty for BMS restenosis compared with DES restenosis. In de-novo lesions (small vessels), TLR rate was 1.0% with PCB alone and 2.4% in patients with additional BMS implantation. These registry results confirm a low rate of TLR with PCB, especially for the treatment of BMS restenosis.

INTERVENTIONAL CARDIOLOGY

DEB for the Treatment of Superficial Femoral Artery ISR **1739**

Eugenio Stabile, Vittorio Virga, Luigi Salemme, Angelo Cioppa, Vittorio Ambrosini, Giovanni Sorropago, Tullio Tesorio, Linda Cota, Grigore Popusoi, Armando Pucciarelli, Giancarlo Biamino, Paolo Rubino

The use of drug-eluting balloons (DEBs) has shown promising results in reducing restenosis in coronary stents. This prospective registry evaluated the safety and efficacy of DEB for the treatment of superficial femoral artery (SFA) in-stent restenosis (ISR). A total of 39 consecutive patients were treated for SFA ISR with final post-dilation with paclitaxel-eluting balloons. Primary patency rate at 12 months was 92%, and all patients were asymptomatic for claudication. These results suggest that adjunctive use of DEB for the treatment of SFA ISR can reduce the risk of recurrent restenosis, but a randomized trial is needed.

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INTERVENTIONAL CARDIOLOGY

Predictive Factors and Long-Term Consequences of LBBB Branch Block Following TAVI With a Balloon-Expandable Valve 1743

Marina Urena, Michael Mok, Vicenc Serra, Eric Dumont, Luis Nombela-Franco, Robert DeLarochellière, Daniel Doyle, Albert Igual, Eric Larose, Ignacio Amat-Santos, Mélanie Côté, Hug Cuéllar, Philippe Pibarot, Peter de Jaegere, François Philippon, Bruno Garcia del Blanco, Josep Rodés-Cabau

Urena and colleagues reviewed records from over 200 subjects who underwent transcatheter aortic valve implantation (TAVI) with a balloon-expandable valve (BEV) to determine if there are any predictive factors for new-onset persistent left bundle branch block (LBBB) after the procedure. New-onset LBBB was observed in approximately one-third of patients immediately after TAVI, and had resolved in 38% and 57% of them at hospital discharge and at 6- to 12-month follow-up, respectively. Baseline QRS duration and prosthesis ventricular depth were independent predictors of persistent LBBB. Patients with persistent LBBB and who did not undergo permanent pacemaker implantation (PPI) prior to hospital discharge had a higher incidence of syncope (16.0% vs. 0.7%, $p = 0.001$) and complete AVB requiring PPI (20.0% vs. 0.7%, $p < 0.001$), but not of global mortality, cardiac mortality, or sudden death.

Editorial Comment: Antonio Colombo, Azeem Latib, p. 1753

MYOCARDIAL INFARCTION

Perceived Stress Associated With Risk of Death After Myocardial Infarction 1756

Suzanne V. Arnold, Kim G. Smolderen, Donna M. Buchanan, Yan Li, John A. Spertus

In a cohort of 4,204 acute myocardial infarction (AMI) patients from 24 U.S. hospitals, Arnold and colleagues had subjects complete the Perceived Stress Scale-4 during hospitalization. AMI patients with moderate/high stress had increased 2-year mortality compared to those having low levels of stress (12.9% vs. 8.6%). This association persisted after adjusting for sociodemographics, clinical factors (including depressive symptoms), revascularization status, and GRACE discharge risk scores. Moderate/high stress at the time of an AMI increases the risk of subsequent mortality.

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HEART FAILURE

The LVAD Ramp Study 1764

Nir Uriel, Kerry A. Morrison, Arthur R. Garan, Tomoko Kato, Melana Yuzefpolskaya, Farhana Latif, Susan W. Restaino, Donna M. Mancini, Margaret Flannery, Hiroo Takayama, Ranjit John, Paolo C. Colombo, Yoshifumi Naka, Ulrich P. Jorde

Uriel and colleagues developed a standardized clinical ramp test protocol to be done at the time of hospital discharge for speed optimization or if device malfunction is suspected in patients with a continuous-flow left ventricular assist device. During echocardiography, the speed of the device is increased in 400 rpm increments. Measurements collected include the slopes (change in x/y on a graph) of the left ventricular end-diastolic dimension, pulsatility index, and power at increasing speeds. The standardized ramp test was found to be both safe and feasible. Speed changes were made in 61% of patients when the test was performed for speed optimization. The test was found to be highly sensitive and specific for the detection of device thrombosis.

Editorial Comment: Joseph G. Rogers, Carmelo A. Milano, p. 1776

HEART FAILURE

Peripheral Endothelial Dysfunction Linked to Prognosis in Patients With HFNEF 1778

Eiichi Akiyama, Seigo Sugiyama, Yasushi Matsuzawa, Masaaki Konishi, Hiroyuki Suzuki, Toshimitsu Nozaki, Keisuke Ohba, Junichi Matsubara, Hirofumi Maeda, Yoko Horibata, Kenji Sakamoto, Koichi Sugamura, Megumi Yamamuro, Hitoshi Sumida, Koichi Kaikita, Satomi Iwashita, Kunihiko Matsui, Kazuo Kimura, Satoshi Umemura, Hisao Ogawa

Akiyama and colleagues investigated whether peripheral endothelial dysfunction could predict the risk of cardiovascular events in patients with heart failure with normal left ventricular ejection fraction (HFNEF). Peripheral endothelial function was assessed noninvasively as the reactive hyperemia index (RHI) using peripheral arterial tonometry (RH-PAT). Kaplan-Meier analysis demonstrated a significantly higher probability of cardiovascular events in the low-RHI group than in the high-RHI group. Peripheral endothelial dysfunction was independently associated with the risk of cardiovascular events in HFNEF patients.

Editorial Comment: Carolyn S. P. Lam, Dirk L. Brutsaert, p. 1787

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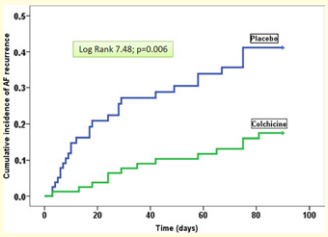

HEART RHYTHM DISORDERS

Colchicine Prevents Early AF Recurrence After Pulmonary Vein Isolation **1790**

Spyridon Deftereos, Georgios Giannopoulos, Charalambos Kossyvakis, Michael Efremidis, Vasiliki Panagopoulou, Andreas Kaoukis, Konstantinos Raisakis, Georgios Bouras, Christos Angelidis, Andreas Theodorakis, Metaxia Driva, Konstantinos Doudoumis, Vlasios Pyrgakis, Christodoulos Stefanadis

Deftereos and colleagues tested the utility of colchicine, an agent with potent anti-inflammatory action, to reduce atrial fibrillation (AF) recurrence after pulmonary vein isolation in patients with paroxysmal AF. After radiofrequency ablation treatment, subjects were randomized to a 3-month course of colchicine, 0.5 mg twice daily, or placebo. Recurrence of AF was observed in 33% of patients in the placebo group compared to 16% of patients who received colchicine. These results suggest that colchicine is an effective and safe treatment for prevention of early AF recurrences after pulmonary vein isolation.

Editorial Comment: Gregory M. Marcus, Jonathan C. Hsu, p. 1797

HEART RHYTHM DISORDERS

Elevated Pre-Operative Serum Peptides for Collagen I and III Synthesis Associated With Post-Surgical AF **1799**

Michael F. Swartz, Gregory W. Fink, Muhammad F. Sarwar, George L. Hicks, Yao Yu, Rui Hu, Charles J. Lutz, Steven M. Taffet, José Jalife

Swartz and colleagues recently demonstrated that the risk of atrial fibrillation (AF) after cardiac surgery is predicted by the degree of left atrial (LA) fibrosis. This study sought to determine if serum markers for collagen I and III synthesis, the C-terminal peptide from pro-collagen-I (PICP) and the N-terminal peptide from pro-collagen III (PIIINP), correlate with LA fibrosis and post-operative AF. A total of 54 patients having cardiac surgery without a history of AF consented to left and right atrial biopsies, and a pre-operative peripheral blood draw. LA mRNA transcripts for collagen I, III, transforming growth factor, and angiotensin were 1.5- to −2.0-fold higher in AF patients. Serum PICP and PIIINP levels were higher in AF versus NSR. This study confirms that serum PICP and PIIINP levels correlate with the presence of left atrial fibrosis and predict the risk of post-operative AF.

Editorial Comment: Jonathan M. Kalman, Saurabh Kumar, Prashanthan Sanders, p. 1807

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HEART RHYTHM DISORDERS

CRT Reduces the Risk of Ventricular Tachyarrhythmic Events in MADIT-CRT 1809

Gregory Ouellet, David T. Huang, Arthur J. Moss, W. Jackson Hall, Alon Barsheshet, Scott McNitt, Helmut Klein, Wojciech Zareba, Ilan Goldenberg

Ouellet and colleagues evaluated the effect of cardiac resynchronization therapy with defibrillator (CRT-D) on the risks of first and recurrent ventricular tachyarrhythmic events (VTE) in MADIT-CRT. Multivariate analysis showed that CRT-D was associated with a 29% reduction in the risk of a first VTE, with a pronounced effect among patients with LBBB (hazard ratio [HR]: 0.58) and no significant effect among non–LBBB patients (HR: 1.05). Patients with LBBB who experienced a first VTE had no change in the risk of subsequent VTEs with CRT-D, but this risk was increased in non–LBBB patients. CRT-D was associated with a significant reduction in the risk of life-threatening VTEs, but does not reduce the risk of subsequent VTEs in patients who experience a first arrhythmic event, and may increase subsequent arrhythmic risk in non–LBBB patients.

HEALTH SERVICES RESEARCH

The Impact of Reducing Cardiovascular Medication Copayments on Health Spending and Resource Utilization 1817

Niteesh K. Choudhry, Michael A. Fischer, Jerry L. Avorn, Joy L. Lee, Sebastian Schneeweiss, Daniel H. Solomon, Christine Berman, Saira Jan, Joyce Lii, John J. Mahoney, William H. Shrank

Reducing copayments for post-myocardial infarction secondary prevention has beneficial effects, but the impact of this strategy for lower-risk patients remains unclear. Choudhry and colleagues evaluated health care spending and resource use by a large self-insured employer that reduced statin copayments for patients with diabetes or vascular disease and reduced clopidogrel copayments for all patients prescribed this drug. Eligible individuals in the intervention company (n = 3,513) were compared to a control group from other companies without such a policy (n = 49,803). Lowering copayments was associated with significant reductions in rates of physician visits and hospitalizations/emergency department admissions, but not major coronary events. Lowering copayments for statins and clopidogrel was associated with reductions in health care resource use and patient out-of-pocket spending, and was cost-neutral with respect to overall health spending.

Editorial Comment: Eric C. Stecker, Eric M. Riles, A. Mark Fendrick, p. 1825

CARDIAC IMAGING

Rb-82 PET Has Superior Accuracy to SPECT for the Diagnosis of Obstructive CAD 1828

Brian A. Mc Ardle, Taylor F. Dowlsey, Robert A. deKemp, George A. Wells, Rob S. Beanlands

Positron emission tomography (PET) using rubidium (Rb)-82 has potential advantages over single-photon emission tomography (SPECT) that may make it more accurate and that reduce radiation exposure compared to SPECT. Mc Ardle and colleagues performed a systematic review of studies where either Rb-82 PET or technetium-99m SPECT with both attenuation correction and ECG-gating were used with invasive coronary angiography (ICA) as the reference standard. A total of 15 PET and 8 SPECT studies (n = 1,344 and n = 1,755, respectively) were included. The sensitivities for PET and SPECT were 90% and 85% with specificities of 88% and 85%, respectively. Rb-82 PET appears to be more accurate for the detection of obstructive CAD than SPECT using current technology.